REMARKS

Claims 109 and 113-213 are pending in the application. Claims 109, 113, and 114 have been amended. Claims 110-112 have been cancelled without prejudice. New claims 180-213 have been added. Support for the amendments and new claims can be found in the specification at, e.g., page 8, line 25, to page 9, line 5. These amendments add no new matter.

Restriction Requirement and Species Election Requirement

At pages 2-4 of the Office Action, the Examiner summarized the species election requirements and the elections made by the undersigned in a telephone conversation on March 16, 2005. For sake of clarity, it is noted that claims 109-179 were pending in the application and claims 1-108 had been cancelled as of the date of the present Office Action (page 2 of the Office Action inadvertently stated that claims 1-117 had been cancelled). Applicants thank the Examiner for extending the prior art search and examination to include all species of antibodies and all species of diseases.

Parent Application No. 09/859,053 (Issued Patent No. 6,803,039)

As discussed in the telephone interview with the Examiners and the undersigned on December 14, 2005, two of the issues raised in the present Office Action were addressed previously during examination of parent Application No. 09/859,053 (issued as Patent No. 6,803,039). The parent patent contains claims to anti-AILIM antibodies. The present application contains claims to methods of using anti-AILIM antibodies having the same features of the antibodies of the issued parent. As detailed in the following sections, certain conclusions reached by the Office during examination of the parent application also apply to issues raised in the present Office Action.

Title of Application

At page 5 of the Office Action, the Examiner requested that the title be amended to clearly indicate the invention to which the claims are directed. The title has been amended to

read as follows: "METHODS OF USE OF A HUMAN MONOCLONAL ANTIBODY AGAINST A COSTIMULATORY SIGNAL TRANSDUCTION MOLECULE AILIM."

35 U.S.C. §112, First Paragraph (Written Description)

At pages 5-7 of the Office Action, the Examiner rejected claims 109-179 as allegedly containing subject matter that was not described in the specification in such a way that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing. According to the Examiner, "Applicant is not in possession of monoclonal antibodies to a genericallly recited 'human AILIM.'"

As noted above, the anti-human AILIM antibodies recited in the present method claims contain the same limitations as the antibodies of Patent No. 6,803,039 (which issued from parent Application No. 09/859,053). With respect to use of the term "human AILIM," the Office acknowledged during prosecution of the prior application that "although the 'AILIM' polypeptide is also commonly known as 'ICOS', the term 'AILIM' at the time the invention was made was also an art-recognized term" (page 4 of Office Action dated January 13, 2003 from Application No. 09/859,053). Because "AILIM" was an art-recognized term at the time the present application was filed, the skilled person would have understood applicants to have been in possession of human monoclonal antibodies (or portions thereof) that bind to human AILIM and have the specific features recited in the claims. In view of these comments, applicants request that the Examiner withdraw the rejection.

35 U.S.C. §112, First Paragraph (Enablement)

At pages 10-11 of the Office Action, the Examiner rejected claims 113, 114, 116, 117, 123, 124, 154, and 155 as allegedly not enabled. According to the Examiner,

> the specification, while being enabling for methods of utilizing antibodies of the specified amino acid sequences, does not reasonably provide enablement for methods of utilizing antibodies "in which one to ten amino acid residues are deleted, substituted, or added." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

practice the invention commensurate in scope with these claims.

As noted above, the anti-human AILIM antibodies recited in the present method claims contain the same limitations as the antibodies of Patent No. 6,803,039 (which issued from parent Application No. 09/859,053). With respect to the phrase "in which one to ten amino acid residues are deleted, substituted, or added," this claim language was discussed during the prosecution of Application No. 09/859,053 in a telephone interview with Examiner Roark on March 25, 2003. Examiner Roark stated that this claim language would not result in an enablement rejection (and no such rejection followed the introduction of this language). In support of the position that antibodies in which one to ten amino acid residues are deleted, substituted, or added can maintain their binding function, enclosed is a copy of a publication of Saviranta et al. (1998) Protein Engineering 11(2):143-52 demonstrating that random, whole domain mutagenesis of the V_H domain resulted in mutant clones that were mainly unchanged in their affinity for estradiol. This supporting publication was also provided to Examiner Roark and discussed during the interview of March 25, 2003 for Application No. 09/859,053. In view of these comments, applicants request that the Examiner withdraw the rejection.

At pages 7-9 of the Office Action, the Examiner rejected claims 109-114 and 118-148 as allegedly not enabled.

As amended, claims 109, 113, and 114 (the independent claims rejected herein) are directed to methods of treating an inflammatory disorder (references to disorders other than an inflammatory disorder have been removed from the claims). Applicants reserve the right to pursue subject matter cancelled from these claims in separate divisional or continuation applications.

The present application contains *in vitro* experimental findings demonstrating that anti-AILIM antibodies inhibit T cell activity (Example 8) and inhibit T cell proliferation (Example 15). The application also describes the *in vivo* use of anti-AILIM antibodies to inhibit delayed-type hypersensitivity in monkeys (Example 11). In addition to the experimental findings contained in the present application, prior Application No. 10/301,056 of Tamatani et al.

(published as US20030083472; copy enclosed; assigned to the assignee of the present application) describes the use of anti-AILIM antibodies in animal models of experimental allergic encephalomyelitis (Example 14) and glomerulonephritis (Example 15).[1]

In view of the disclosure contained in the present application combined with the knowledge in the art (including the above-mentioned disclosure of Application No. 10/301,056) at the time the present application was filed, the skilled person would have been able to carry out the claimed methods without undue experimentation and with a reasonable expectation of success. Consistent with the foregoing assertions, the Office previously found the following claim of Application No. 10/301,056 to be allowable.

> 70. A method of treating an inflammatory disease in a subject, the method comprising administering to the subject an effective amount of a pharmaceutical composition comprising (i) a pharmaceutically acceptable carrier and (ii) a monoclonal antibody that binds to a polypeptide consisting of SEQ ID NO:2.[2]

In finding the above claim of Application No. 10/301,056 allowable (which claim was directed to the use of a generic anti-human AILIM antibody), the Office stated at page 2 of the Communication of December 17, 2003 that "besides the working Examples of treating inflammation in animal models provided in the instant specification, others also teach that antibodies to ICOS (the current name in the art for the AILIM polypeptide) can be used to treat inflammatory disease in a subject."[3] Applicants respectfully submit that this same rationale applies to the present, later-filed application, the claims of which are directed to the use of an anti-AILIM antibody or portion thereof (having the specific features recited in the claims) for the treatment of an inflammatory disorder.

A publication of Tezuka et al. (US20040229790; copy enclosed) further confirms the effectiveness of anti-AILIM antibodies for treating inflammation in general and arthritis in particular. For example, Tezuka et al. describes the *in vivo* use of anti-AILIM antibodies in animal models of arthritis (Example 4) and hepatitis (Example 5).

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[1] The specification of Application No. 10/301,056 was publicly available (as corresponding PCT publication Number WO 98/38216, published September 3, 1998) as of the earliest claimed priority date of the present application.
[2] SEQ ID NO:2 is human AILIM.
[3] Application No. 10/301,056 was subsequently abandoned.

In view of the foregoing comments, applicants request that the Examiner withdraw the rejection.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are in condition for allowance, which action is earnestly requested.

Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 14539-006002.

Respectfully submitted,

Date: February 14, 2006

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